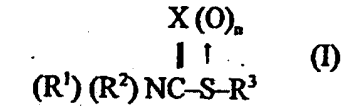
WHAT IS CLAIMED IS:

1. A therapeutic method comprising preventing or treating a glutamate-related disorder in a mammal, by administering to said mammal an effective amount of a compound of the formula I:



(I)

wherein

a) R^1 and R^2 are individually $(C_1\text{-}C_8)$ alkyl, $(C_6\text{-}C_{12})$aryl, or heteroaryl; or R^1 and R^2 together with the nitrogen to which they are attached are a 4-8 membered ring optionally comprising 1, 2, or 3 additional heteroatoms selected from the group consisting of non-peroxide oxygen, sulfur, and $N(R_a)$, wherein each R_a is absent or is hydrogen, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$alkanoyl, phenyl, benzyl, or phenethyl; and R^3 is hydrogen, $(C_1\text{-}C_8)$alkyl, $(C_6\text{-}C_{12})$aryl, heteroaryl, $SC(=S)N(R^1)(R^2)$, or a glutathione derivative; or

b) R^1 and R^3 together are a divalent ethylene or propylene chain and R^2 is $(C_1\text{-}C_8)$ alkyl, $(C_6\text{-}C_{12})$aryl, or heteroaryl; or

c) R^1 and R^2 together with the nitrogen to which they are attached are an azetidino, pyrrolidino, piperidino, hexamethyleneimin-1-yl, or heptamethylene-imin-1-yl ring, said ring being substituted on carbon by a substituent R_b; wherein R_b and R^3 taken together are methylene ($-CH_2-$), ethylene ($-CH_2CH_2-$), or a direct bond; and wherein the ring comprising R_b and R^3 is a five- or a six-membered ring;

wherein any aryl or heteroaryl in R^1, R^2, or R^3 may optionally be substituted with 1, 2, or 3 substituents selected from the group consisting of halo, nitro, cyano, hydroxy, $(C_1\text{-}C_8)$alkoxy, $(C_1\text{-}C_8)$alkanoyl, $(C_2\text{-}C_8)$alkanoyloxy, trifluoromethyl, trifluoromethoxy, and carboxy;

X is O or S; and

n is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof.

2. The method of claim 1 wherein the glutamate-related disorder is a neurodegenerative disease.

3. The method of claim 2, wherein the neurodegenerative disease Huntington's disease, Alzheimer's disease, Parkinson's disease, aquired immunodeficiency syndrome (AIDS), epilepsy, nicotine addiction, cerebral ischemia, or familial Amyotrophic Lateral Sclerosis (ALS).

4. The method of claim 2, wherein the neurodegenerative disease is Wernicke-Korsakoff syndrome, cerebral beriberi, Machado-Joseph disease, or Soshin disease.

5. The method of claim 1 wherein the glutamate-related disorder is anxiety, glutamate related convulsions, hepatic encephalopathy, neuropathic pain, domoic acid poisoning, hypoxia, anoxia, mechanical trauma to the nervous system, hypertension, alcohol withdrawal seizures, alcohol addiction, alcohol craving, cardiovascular ischemia, oxygen convulsions, or hypoglycemia.

6. The method of claim 1 wherein the glutamate-related disorder is anxiety, glutamate related convulsions, hepatic encephalopathy, domoic acid poisoning, hypoxia, anoxia, alcohol withdrawal seizures, alcohol addiction, alcohol craving, oxygen convulsions, or hypoglycemia.

7. The method of claim 1 wherein the glutamate-related disorder is anxiety.

8. The method of claim 1 wherein the glutamate-related disorder is glutamate related convulsions.

9. The method of claim 1 wherein the glutamate-related disorder is alcohol withdrawal seizures.

10. The method of claim 1 wherein the glutamate-related disorder is alcohol addiction.

11. The method of claim 1 wherein the glutamate-related disorder is alcohol craving.

12. The method of claim 1 wherein the glutamate-related disorder is oxygen convulsions.

13. The method of claim 1 wherein the glutamate-related disorder is neuropathic pain.

14. The method of claim 1 wherein the glutamate-related disorder is Huntington's disease.

15. The method of claim 1 wherein the glutamate-related disorder is cerebral ischemia.

16. The method of claim 1 wherein the glutamate-related disorder is epilepsy.

17. The method of any one of claims 1 to 16 wherein the compound is S-methyl-N,N-diethylthiolcarbamate sulfoxide.

18. The method of any one of claims 1 to 16 wherein the compound is S-methyl-N,N-diethyldithiocarbamate sulfoxide.

19. The method of any one of claims 1 to 16 wherein the compound is S-methyl-N,N-dimethylthiolcarbamate sulfoxide.

20. The method of any one of claims 1 to 16 wherein the compound is S-methyl-N,N-dipropylthiolcarbamate sulfoxide.

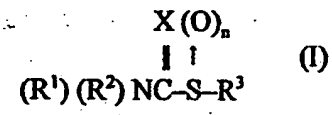
21. The method of any one of claims 1 to 16 wherein R^1=R^2=ethyl.

22. The method of any one of claims 1 to 16 wherein X is O.

23. The method of any one of claims 1 to16 wherein X is S.

24. The method of any one of claims 1 to 16 wherein R^1 and R^2 are individually $(C_1$-$C_8)$alkyl or $(C_6$-$C_{12})$aryl; R^3 is $(C_1$-$C_8)$ alkyl, H, SC(=S)N(R^1)(R^2) or a glutathione derivative; X is O or S; and n is 0 or 1, or a pharmaceutically acceptable salt thereof.

25. A method comprising inhibiting or preventing glutamate binding to mammalian neurotransmitter receptors, by contacting mammalian tissue comprising said receptors with an amount of a compound of formula (I):



(I)

wherein

a) R^1 and R^2 are individually $(C_1$-$C_8)$ alkyl, $(C_6$-$C_{12})$aryl, or heteroaryl; or R^1 and R^2 together with the nitrogen to which they are attached are a 4-8 membered ring optionally comprising 1, 2, or 3 additional heteroatoms selected from the group consisting of non-peroxide oxygen, sulfur, and N(R_a), wherein each R_a is absent or is hydrogen, $(C_1$-$C_8)$alkyl, $(C_1$-$C_8)$alkanoyl, phenyl, benzyl, or phenethyl; and R^3 is hydrogen, $(C_1$-$C_8)$alkyl, $(C_6$-$C_{12})$aryl, heteroaryl, SC(=S)N(R^1)(R^2), or a glutathione derivative; or

b) R^1 and R^3 together are a divalent ethylene or propylene chain and R^2 is $(C_1\text{-}C_8)$ alkyl, $(C_6\text{-}C_{12})$aryl, or heteroaryl; or

c) R^1 and R^2 together with the nitrogen to which they are attached are an azetidino, pyrrolidino, piperidino, hexamethyleneimin-1-yl, or heptamethylene-imin-1-yl ring, said ring being substituted on carbon by a substituent R_b; wherein R_b and R^3 taken together are methylene ($-CH_2-$), ethylene ($-CH_2CH_2-$), or a direct bond; and wherein the ring comprising R_b and R^3 is a five- or a six-membered ring;

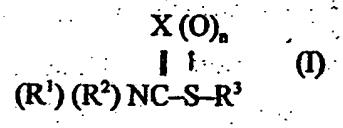
wherein any aryl or heteroaryl in R^1, R^2, or R^3 may optionally be substituted with 1, 2, or 3 substituents selected from the group consisting of halo, nitro, cyano, hydroxy, $(C_1\text{-}C_8)$alkoxy, $(C_1\text{-}C_8)$alkanoyl, $(C_2\text{-}C_8)$alkanoyloxy, trifluoromethyl, trifluoromethoxy, and carboxy;

X is O or S; and

n is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof; wherein the amount is effective to block or reduce the binding of glutamate to said receptors.

26. A compound of formula I:



(I)

wherein

a) R^1 and R^3 together are a divalent ethylene or propylene chain and R^2 is $(C_1\text{-}C_8)$ alkyl, $(C_6\text{-}C_{12})$aryl, or heteroaryl; or

b) R^1 and R^2 together with the nitrogen to which they are attached are an azetidino, pyrrolidino, piperidino, hexamethyleneimin-1-yl, or heptamethylene-imin-1-yl ring, said ring being substituted on carbon by a substituent R_b; wherein R_b and R^3 taken together are methylene ($-CH_2-$), ethylene ($-CH_2CH_2-$), or a direct

bond; and wherein the ring comprising R_b and R^3 is a five- or a six-membered ring;

wherein any aryl or heteroaryl in R^1, R^2, or R^3 may optionally be substituted with 1, 2, or 3 substituents selected from the group consisting of halo, nitro, cyano, hydroxy, (C_1-C_8)alkoxy, (C_1-C_8)alkanoyl, (C_2-C_8)alkanoyloxy, trifluoromethyl, trifluoromethoxy, and carboxy;

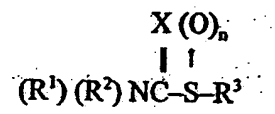
X is O or S; and

n is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof.

27. A pharmaceutical composition comprising a compound of claim 26 and a pharmaceutically acceptable carrier.

28. The use of a compound of formula (I):



(I)

wherein

a) R^1 and R^2 are individually (C_1-C_8) alkyl, (C_6-C_{12})aryl, or heteroaryl; or R^1 and R^2 together with the nitrogen to which they are attached are a 4-8 membered ring optionally comprising 1, 2, or 3 additional heteroatoms selected from the group consisting of non-peroxide oxygen, sulfur, and N(R_a), wherein each R_a is absent or is hydrogen, (C_1-C_8)alkyl, (C_1-C_8)alkanoyl, phenyl, benzyl, or phenethyl; and R^3 is hydrogen, (C_1-C_8)alkyl, (C_6-C_{12})aryl, heteroaryl, SC(=S)N(R^1)(R^2), or a glutathione derivative; or

b) R^1 and R^3 together are a divalent ethylene or propylene chain and R^2 is (C_1-C_8) alkyl, (C_6-C_{12})aryl, or heteroaryl; or

c) R^1 and R^2 together with the nitrogen to which they are attached are an azetidino, pyrrolidino, piperidino, hexamethyleneimin-1-yl, or

heptamethylene-imin-1-yl ring, said ring being substituted on carbon by a substituent R_b; wherein R_b and R^3 taken together are methylene (-CH_2-), ethylene (-CH_2CH_2-), or a direct bond; and wherein the ring comprising R_b and R^3 is a five- or a six-membered ring;

wherein any aryl or heteroaryl in R^1, R^2, or R^3 may optionally be substituted with 1, 2, or 3 substituents selected from the group consisting of halo, nitro, cyano, hydroxy, (C_1-C_8)alkoxy, (C_1-C_8)alkanoyl, (C_2-C_8)alkanoyloxy, trifluoromethyl, trifluoromethoxy, and carboxy;

X is O or S; and

n is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof; to prepare a medicament useful to treat a glutamate-related disorder.

29. The use of claim 28 wherein the glutamate-related disorder is a neurodegenerative disease.

30. The use of claim 29, wherein the neurodegenerative disease Huntington's disease, Alzheimer's disease, Parkinson's disease, aquired immunodeficiency syndrome (AIDS), epilepsy, nicotine addiction, cerebral ischemia (stroke), or familial Amyotrophic Lateral Sclerosis (ALS).

31. The use of claim 29, wherein the neurodegenerative disease is Wernicke-Korsakoff syndrome, cerebral beriberi, Machado-Joseph disease, or Soshin disease.

32. The use of claim 28 wherein the glutamate-related disorder is anxiety, glutamate related convulsions, hepatic encephalopathy, neuropathic pain, domoic acid poisoning, hypoxia, anoxia, mechanical trauma to the nervous system, hypertension, alcohol withdrawal seizures, alcohol addiction, alcohol craving, cardiovascular ischemia, oxygen convulsions, or hypoglycemia.

33. The use of claim 28 wherein the glutamate-related disorder is anxiety, glutamate related convulsions, hepatic encephalopathy, domoic acid poisoning, hypoxia, anoxia, alcohol withdrawal seizures, alcohol addiction, alcohol craving, oxygen convulsions, or hypoglycemia.

34. The use of claim 28 wherein the glutamate-related disorder is anxiety.

35. The use of claim 28 wherein the glutamate-related disorder is glutamate related convulsions.

36. The use of claim 28 wherein the glutamate-related disorder is alcohol withdrawal seizures.

37. The use of claim 28 wherein the glutamate-related disorder is alcohol addiction.

38. The use of claim 28 wherein the glutamate-related disorder is alcohol craving.

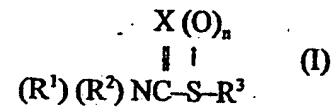
39. The use of claim 28 wherein the glutamate-related disorder is oxygen convulsions.

40. The use of claim 28 wherein the glutamate-related disorder is neuropathic pain.

41. The use of claim 28 wherein the glutamate-related disorder is cerebral ischemia.

42. The use of claim 28 wherein wherein the glutamate-related disorder is epilepsy.

43. A compound of formula I:



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wherein

a) R^1 and R^3 together are a divalent ethylene or propylene chain and R^2 is $(C_1\text{-}C_8)$ alkyl, $(C_6\text{-}C_{12})$aryl, or heteroaryl; or

b) R^1 and R^2 together with the nitrogen to which they are attached are an azetidino, pyrrolidino, piperidino, hexamethyleneimin-1-yl, or heptamethyleneimin-1-yl ring, said ring being substituted on carbon by a substituent R_b; wherein R_b and R^3 taken together are methylene ($-CH_2-$), ethylene ($-CH_2CH_2-$), or a direct bond; and wherein the ring comprising R_b and R^3 is a five- or a six-membered ring;

wherein any aryl or heteroaryl in R^1, R^2, or R^3 may optionally be substituted with 1, 2, or 3 substituents selected from the group consisting of halo, nitro, cyano, hydroxy, $(C_1\text{-}C_8)$alkoxy, $(C_1\text{-}C_8)$alkanoyl, $(C_2\text{-}C_8)$alkanoyloxy, trifluoromethyl, trifluoromethoxy, and carboxy;

X is O or S; and

n is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof; for use in medical therapy.

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Date of Deposit: October 28, 2002
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